

88. (new) The mononuclear phagocyte according to claim 87 wherein expression of the NOI is regulated by the regulatable element at a target hypoxia and/or ischemic and/or stress site.


89. (new) The mononuclear phagocyte according to claim 87 or claim 88 wherein the mononuclear phagocyte further comprises a binding agent capable of binding to a cell surface element of the mononuclear phagocyte.

90. (new) The mononuclear phagocyte according to claim 89 wherein the binding agent comprises a ligand adapted to bind to the cell surface element of the mononuclear phagocyte, preferably wherein the ligand is a mannosylated poly - L - lysine.

91. (new) The mononuclear phagocyte according to claim 89 wherein the binding agent comprises a viral vector for internalising the regulatable agent into the mononuclear phagocyte.

92. (new) The mononuclear phagocyte according to claim 87 wherein the NOI is incorporated into the genome of the mononuclear phagocyte.

93. (new) The mononuclear phagocyte according to claim 91 wherein the viral vector is a lentiviral vector.

94. (new) The mononuclear phagocyte according to claim 92 wherein the viral vector is a lentiviral vector. 

95. (new) The mononuclear phagocyte according to claim 91 wherein the viral vector is an adenoviral vector.

96. (new) The mononuclear phagocyte according to claim 87 wherein at least one NOI encodes a pro-drug activation enzyme.

97. (new) The mononuclear phagocyte according to claim 87 wherein the mononuclear phagocyte further comprises a bioreductively activated pro-drug.

98. (new) The mononuclear phagocyte according to claim 87 wherein the regulatable element comprises a hypoxic response element (HRE).

99. (new) The mononuclear phagocyte according to claim 87 wherein the regulatable element comprises an inducible or repressible promoter element.

100. (new) The mononuclear phagocyte according to claim 99 wherein the inducible or repressible promoter element comprises a tetracycline repressor DNA sequence.

101. (new) The mononuclear phagocyte according to claim 87 wherein the mononuclear phagocyte further comprises an NOI encoding an activating or control product.

102. (new) The mononuclear phagocyte according to claim 101 wherein the activating product is HIF1-alpha. F

103. (new) The mononuclear phagocyte according to claim 101 wherein the control product is a tetracycline repressor protein. F

104. (new) The mononuclear phagocyte according to claim 87 wherein the mononuclear phagocyte further comprises an NOI encoding a protein that kills mononuclear phagocytes.

105. (new) A method for selectively destroying a mononuclear phagocyte comprising:  
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providing the mononuclear phagocyte according to claim 104; and

exposing said mononuclear phagocyte to hypoxic and/or ischemic and/or stress conditions that occur either artificially by induction or occur/exist naturally; such that the mononuclear phagocyte is selectively destroyed after expression of the cytotoxic, hypoxially and/or ischemically and/or stress activated agent at the target hypoxic and/or ischemic and/or stress site.

106. (new) A method for targeting a mononuclear phagocyte to hypoxic and/or ischemic and/or stress sites comprising;

providing a mononuclear phagocyte as defined claim 87; and

allowing said mononuclear phagocyte to migrate under conditions that support migration to a hypoxic and/or ischemic and/or stress site either *in vitro* or *in vivo*.

107. (new) A method for treating a condition associated with hypoxic and/or ischemic and/or stress state comprising administering to an individual to be treated a mononuclear phagocyte according claim 87.

108. (new) A method for treating a condition associated with a hypoxic and/or ischemic and/or stress state comprising;

withdrawing blood and/or serum from an individual to be treated;

treating said blood and/or serum *in vitro* with a mononuclear phagocyte according to claim 87; and

re-injecting said treated blood and/or serum into the individual either systemically or directly into a hypoxic and/or ischemic and/or stress area.

109. (new) A delivery system for targeting a mononuclear phagocyte according to claim 87 to a target hypoxic and/or ischemic and/or stress site.

110. (new) The mononuclear phagocyte according to claim 87 wherein the hypoxic and/or ischemic and/or stress associated condition is a tumour associated condition.

111. (new) A construct comprising at least one regulatable element operably linked to at least one nucleotide sequence of interest (NOI), wherein said regulatable element is selected from a hypoxia regulatable element, an ischemic regulatable element and a stress regulatable element, and wherein the construct is coupled to a binding agent that is capable of binding to a cell surface element of a mononuclear phagocyte.

112. (new) The construct according to claim 111 wherein the regulatable element is an HRE element.

113. (new) The construct according to claim 111 or claim 112 wherein the binding agent

114. (new) The construct according to claim 111 or claim 112 wherein the binding agent comprises a viral vector for internalising the regulatable element into a mononuclear phagocyte.

115. (new) The construct according to claim 114 wherein the viral vector is selected from the group consisting of an adenoviral vector and a lentiviral vector.

116. (new) A method for internalising a regulatable element into a mononuclear phagocyte wherein the regulatable element is selected from a hypoxia regulatable element, an ischemic regulatable element and a stress regulatable element and the method comprises:

providing a mononuclear phagocyte; and

exposing the mononuclear phagocyte to a construct as defined in any one of claims 111 or 112 under conditions sufficient to internalise the construct into the mononuclear phagocyte.

117. (new) A method for treating a condition associated with hypoxic and/or ischemic and/or stress state comprising administering to an individual to be treated a construct according to any one of claims 111 or 112.

118. (new) A method for treating a condition associated with a hypoxic and/or ischemic and/or stress state comprising;

withdrawing blood and/or serum from an individual to be treated;

treating said blood and/or serum *in vitro* with a construct according to any one of claims 111 or 112; and

re-injecting said treated blood and/or serum into the individual either systemically or directly into a hypoxic and/or ischemic and/or stress area.

119. (new) A method according to claim 117 wherein the condition is a tumour associated condition.

120. (new) A pharmaceutical composition comprising a mononuclear phagocyte according to claim 87 optionally admixed with a pharmaceutically acceptable diluent, excipient or carrier.

121. (new) A pharmaceutical composition comprising a construct according to claim 87 optionally admixed with a pharmaceutically acceptable diluent, excipient or carrier.

122. (new) A mononuclear phagocyte comprising an NOI encoding a p450 enzyme wherein the NOI has been internalised into the mononuclear phagocyte by an adenoviral vector.

a hypoxia response element (HRE); such that the p450 enzyme is expressed under conditions that occur either artificially by induction or occur/exist naturally.

123. (new) The mononuclear phagocyte according to claim 96 wherein the pro-drug activation enzyme is a p450 enzyme.

124. (new) The mononuclear phagocyte according to claim 123 wherein the p450 enzyme, is a CYP2B6 p450 enzyme.

125. (new) The construct according to claim 113 wherein the ligand is a mannosylated poly - L -lysine.

126. (new) A method according to claim 118 wherein the condition is a tumour associated condition.-- E

#### REMARKS

Reconsideration is requested.

Claims 51-86 have been canceled, without prejudice. Claims 87-126 have been added and are pending. The pending claims find support throughout the specification. The claims have been rewritten in response also to the Examiner's request on page 15 of the Office Action of November 8, 2001 (Paper No. 14), for a clean copy of all the